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EXAMINER	
CROUCH, DEBORAH	

ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/809,738	STICE, STEVEN	
	Examiner	Art Unit	
	Deborah Crouch, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-10 and 12-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-10,12-14,16-19 and 23-30* is/are rejected.

7)☒ Claim(s) *15, 20-22 and 31-34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Applicant's arguments filed June 16, 2008 have been fully considered but they are not persuasive. The amendment has been entered. Claims 1-5, 7-10 and 12-34 are pending

Claim 15 and 20-22 would be allowable if written in independent claims. Presently they are objected to as depending from a rejected independent claim.

Comment: The claim limitation " cloned nonhuman, nonprimate mammal" is redundant. Applicant may delete "nonhuman" and have the same scope.

Applicant is advised that should claims 15-22 be found allowable, claims 31-34 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

The response to Applicant's arguments regarding the obviousness rejections is below.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7, 9, 10, 14, 16, 17, 19 and 23-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1998) Science, Vol. 280, pp. 1256-1258

OR Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013.

Cibelli teaches the production of cow embryos by nuclear transfer, where a fibroblast cell transfected with a nucleic acid construct comprising the genes for β-galactosidase and neo^r was electrofused with enucleated MII arrested oocyte and activated (page 1256, col. 3, parag. 1, lines 1-8 and page 1257, col. 1, parag. 2). Of 28 NT embryos transferred to surrogate mothers, 4 calves were born, a success rate of 14%. Electrofusion is a form of artificial activation.

Prather teaches the production of pig embryos by nuclear transfer, where a nucleus from a pig 2-, 4 or 8-cell embryo was transferred into an enucleated MII arrested pig oocyte and electrofused (page 416, col. 1, parag. 1). One piglet was produced after transfer of 88 (42 + 46; ~1%) reconstructed embryos to a surrogate female pig (page 416, col. 2, lines 3-10).

Kwon teaches the production of mouse embryos by nuclear transfer where a karyoplast or isolated nucleus of metaphase embryo cells was introduced into an enucleated MII phase arrested mouse oocyte, fused and electro-activated, an artificial activation method (page 13010, col. 2, parag. 4, lines 1-3). Kwon teaches 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Cibelli offers motivation is stating the cell cycle of the donor in the nuclear transfer experiments is unknown, but the properties of the donor cell are important factors (page 1257, col. 3, parag. 3). Prather offers motivation in stating the cell cycle stage of the embryo that is the donor nucleus may be important in successful cloning

(page 417, col. 2, lines 3-8). Kwon offers motivation in teaching 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Claims 1 and 7-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1998) Science, Vol. 280, pp. 1256-1258 or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 and Wakayama et al (1998) Nature, Vol. 394, pp. 369-374 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013.

Cibelli teaches the production of cow embryos by nuclear transfer, where a fibroblast cell transfected with a nucleic acid construct comprising the genes for β-galactosidase and neo^r was electrofused with enucleated MII arrested oocyte and activated (page 1256, col. 3, parag. 1, lines 1-8 and page 1257, col. 1, parag. 2). Of 28 NT embryos transferred to surrogate mothers, 4 calves were born, a success rate of 14%. Electrofusion is a form of artificial activation.

Prather teaches the production of pig embryos by nuclear transfer, where a nucleus from a pig 2-, 4 or 8-cell embryo was transferred into an enucleated MII arrested pig oocyte and electrofused (page 416, col. 1, parag. 1). One piglet was produced after transfer of 88 (42 + 46; ~1%) reconstructed embryos to a surrogate female pig (page 416, col. 2, lines 3-10).

Wakayama teaches the production of mouse embryos by nuclear transfer, where the nucleus of a cumulus cell was inserted into an enucleated MII arrested oocyte (page

370, col. 1, parag. 1 to page 371, col. 1, parag. 2 col. 3, parag. 1, line 8). Wakayama teaches about 2-3% success rate in producing mice by nuclear transfer.

Kwon teaches the production of mouse embryos by nuclear transfer where a karyoplast or isolated nucleus of metaphase embryo cells was introduced into an enucleated MII phase arrested mouse oocyte, fused and electro-activated, an artificial activation method (page 13010, col. 2, parag. 4, lines 1-3). Kwon teaches 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Cibelli offers motivation is stating the cell cycle of the donor in the nuclear transfer experiments is unknown, but the properties of the donor cell are important factors (page 1257, col. 3, parag. 3). Prather offers motivation in stating the cell cycle stage of the embryo that is the donor nucleus may be important in successful cloning (page 417, col. 2, lines 3-8). Kwon offers motivation in teaching 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Claims 1, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1998) Science, Vol. 280, pp. 1256-1258 or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 and of Campbell et al (1994) Biology of Reproduction, Vol. 50, pp. 1385-1393.

Cibelli teaches the production of cow embryos by nuclear transfer, where a fibroblast cell transfected with a nucleic acid construct comprising the genes for β-galactosidase and neo^r was electrofused with enucleated MII arrested oocyte and activated (page 1256, col. 3, parag. 1, lines 1-8 and page 1257, col. 1, parag. 2). Of 28

NT embryos transferred to surrogate mothers, 4 calves were born, a success rate of 14%. Electrofusion is a form of artificial activation.

Prather teaches the production of pig embryos by nuclear transfer, where a nucleus from a pig 2-, 4 or 8-cell embryo was transferred into an enucleated MII arrested pig oocyte and electrofused (page 416, col. 1, parag. 1). One piglet was produced after transfer of 88 (42 + 46; ~1%) reconstructed embryos to a surrogate female pig (page 416, col. 2, lines 3-10).

Kwon teaches the production of mouse embryos by nuclear transfer where a karyoplast or isolated nucleus of metaphase embryo cells was introduced into an enucleated MII phase arrested mouse oocyte, fused and electro-activated, an artificial activation method (page 13010, col. 2, parag. 4, lines 1-3). Kwon teaches 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Campbell teaches the production of reconstructed nuclear transfer sheep embryos by the transfer of a donor cell nucleus into the cytoplasm of enucleated oocyte and activating at the time of transfer (page 1389, col. 1, Table 2). Campbell also teaches the production of nuclear transfer sheep embryos by transfer of a donor cell nucleus into the cytoplasm of an enucleated activated sheep oocyte (page 1390, col. 2, parag. 2, lines 1-4). Campbell offers motivation for using recipient oocytes activated at the time of donor nucleus transfer or preactivated oocytes in stating unactivated MII oocytes contain high levels of MPF which may be detrimental to the develop of the reconstructed embryo (page 1390, col. 2, parag. 1, lines 5-14). Lambs developed from reconstructed embryos transferred to surrogate mother sheep, but percentages are not

available. Campbell states the decrease in MPF activity in preactivated or activated at the time of transfer prevents abnormal chromosome number in bovine reconstructed oocytes (page 1391, col. 2, lines 1-6).

Claims 1 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cibelli et al (1998) Science, Vol. 280, pp. 1256-1258 or Prather et al. (1989) Biology of Reproduction, Vol. 41, pp. 414-418 in view of Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 Kwon et al. (1996) Proced. Natl. Acad. Sci., Vol. 93, pp. 13010-13013 in view of Yang et al, (1992) Biol. Reprod. 46, suppl. No. 1, page 117, Abs. 268.

Cibelli teaches the production of cow embryos by nuclear transfer, where a fibroblast cell transfected with a nucleic acid construct comprising the genes for β-galactosidase and neo^r was electrofused with enucleated MII arrested oocyte and activated (page 1256, col. 3, parag. 1, lines 1-8 and page 1257, col. 1, parag. 2). Of 28 NT embryos transferred to surrogate mothers, 4 calves were born, a success rate of 14%. Electrofusion is a form of artificial activation.

Prather teaches the production of pig embryos by nuclear transfer, where a nucleus from a pig 2-, 4 or 8-cell embryo was transferred into an enucleated MII arrested pig oocyte and electrofused (page 416, col. 1, parag. 1). One piglet was produced after transfer of 88 (42 + 46; ~1%) reconstructed embryos to a surrogate female pig (page 416, col. 2, lines 3-10).

Kwon teaches the production of mouse embryos by nuclear transfer where a karyoplast or isolated nucleus of metaphase embryo cells was introduced into an

enucleated MII phase arrested mouse oocyte, fused and electro-activated, an artificial activation method (page 13010, col. 2, parag. 4, lines 1-3). Kwon teaches 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Yang teaches methods of activating matured oocytes in the presence of cycloheximide (lines 4-6). Yang teaches that cycloheximide and electrofusion combined resulted in the activation of 90% of the oocytes (lines 20-27).

Cibelli offers motivation is stating the cell cycle of the donor in the nuclear transfer experiments is unknown, but the properties of the donor cell are important factors (page 1257, col. 3, parag. 3). Prather offers motivation in stating the cell cycle stage of the embryo that is the donor nucleus may be important in successful cloning (page 417, col. 2, lines 3-8). Kwon offers motivation in teaching 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Response

Applicant argues with regard to Cibelli or Prather in view of Kwon that nothing in any of these references suggests or motivates the artisan to use differentiated metaphase cells as the donor genetic material. Applicant argues Cibelli discloses using fibroblast cell as the donor genetic material, but does not disclose or suggest the use of metaphase fibroblasts. Applicant argues Kwon discloses a method of nuclear transfer using undifferentiated, embryonic donor cells. Applicant argues the office is inconsistent in relying on motivation in Cibelli as Cibelli states more research is required to for successful reprogramming and live birth of cloned mammals. Applicant further argues Kwon's teaching of a 27% birthrate only motivates the use of Kwon's specific method,

undifferentiated donor material, and does not suggest a feature of Kwon's method that might be the source of Kwon's success rate. Further applicant argues Kwon's use of embryonic cells, which are known in the art to require less reprogramming than differentiated cells. Applicant argues Kwon does not teach or suggest either donor differentiated genetic material or differentiated donor genetic material in any stage of the cell cycle. Applicant argues the ordinary artisan would have been more likely to attribute the success of Kwon to the use of embryonic donor cells, rather than differentiated donor cells as claimed. Applicant argues Prather fails to motivate in saying the cell cycle may be important in successful cloning because Prather would teach away from using differentiated donor material. These arguments are not persuasive.

As stated in the obviousness rejections above, Know shows a 27% increase in the live birthrate when metaphase embryonic donor cells were nuclear donors. The rejection states:

> Kwon teaches the production of mouse embryos by nuclear transfer where a karyoplast or isolated nucleus of metaphase embryo cells was introduced into an enucleated MII phase arrested mouse oocyte, fused and electro-activated, an artificial activation method (page 13010, col. 2, parag. 4, lines 1-3). Kwon teaches 27% of the transferred mouse reconstructed embryos developed to term (page 13012, Table 2).

Thus, applicant's arguments are not persuasive because Kwon teaches nuclear transfer rates of live births increase when a metaphase embryonic cell is used as the nuclear donor. This, in view of Cibelli discussing the importance of the cell cycle in successful cloning and that more research is required to affect effective reprogramming of differentiated donor cells, would motivate the ordinary artisan at the time of filing to

combine the prior art references. All that is required by the claims as presently written is that there be at least one birth. One birth is a reasonable expectation when Cibelli, Kwon and Prather are combined. Further, the ordinary artisan would believe the 27% birth rate is due to the use so metaphase embryonic cells, because Kwon discloses such (Kwon, page 13012, col. 2, parag. 2, line 1 to page 13013, col. 1, line 3). Furthermore, it is maintained that Prather offers motivation in indicating the cell cycle stage of the donor cell maybe important.

In arguing the rejections that include Wakayama, Campbell and Yang, applicant argues that while teaching the specific limitation, none of these references teach the use of a differentiated, metaphase donor nucleus in a nuclear transfer procedure. Applicant's assessment is correct. However, as Kwon is relied upon to teach use of a metaphase donor nucleus and in conjunction with Cibelli, a metaphase differentiated donor nucleus, the combine art provides the teaching, suggestion and motivation to reach the claimed invention. Applicant has not provided any arguments or evidence that the ordinary artisan would have the teachings, suggestion and motivation to combine Cibelli and Kwon at least to perform nuclear transfer using a differentiated metaphase donor cell.

Claims 15, 20-22 and 31-34 are free of the art at the time of filing.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (571)272-0727. The examiner can normally be reached on M-Fri, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Deborah Crouch, Ph.D./
Primary Examiner, Art Unit 1632

September 11, 2008